ORIGINAL ARTICLE

Indocyanine Green-assisted Phacoemulsification in Cases of Complicated or Simple Advanced Cataracts

Yi-Sheng Chang,[1,2] Jing-Hsing Hsiao,[1] Sung-Huei Tseng,[1] Po-Hsiu Kuo,[2] Fred Kuanfu Chen[1]*

Background/Purpose: During phacoemulsification for advanced cataracts, particularly when complicated by anterior segment abnormalities, capsulorhexis is very difficult and carries a high risk of complications. This study investigated the efficacy and safety of indocyanine green (ICG)-assisted phacoemulsification in complicated or simple advanced cataracts.

Methods: Thirty-two patients (35 eyes) underwent phacoemulsification for complicated advanced cataracts (group 1) or simple advanced (mature/hypermature) cataracts (group 2). Anterior segment abnormalities (corneal opacity, small pupil, or glaucoma) in group 1 complicated phacoemulsification. In both groups, 0.5% ICG was used for capsulorhexis, and subsequent procedures were performed in the same routine manner.

Results: Group 1 included 15 patients (17 eyes) with a mean age of 60.0 years. Group 2 included 17 patients (18 eyes) with a mean age of 69.4 years ($p < 0.05$). Continuous curvilinear capsulorhexis was completed in all eyes in group 2, but radial tears occurred in four (23.5%) eyes in group 1 ($p < 0.05$). Phacoemulsification was performed uneventfully in all eyes in both groups. Postoperative complications (corneal edema, vitreous prolapse, posterior capsule opacity, elevated intraocular pressure) were seen in five (27.8%) eyes in group 1 and four (23.5%) eyes in group 2 ($p > 0.05$). None of these were attributed to the use of ICG. Visual acuity improved in all eyes in group 2, but in only 11 (64.7%) in group 1 ($p < 0.01$).

Conclusion: ICG-assisted phacoemulsification is safe and helpful for complicated or simple advanced cataracts. Differences between the two groups in patient age, intraoperative complications, and visual outcome could be explained by differences in the cause(s) of advanced cataracts. [*J Formos Med Assoc* 2008; 107(9):710–719]

Key Words: capsulorhexis, cataract, indocyanine green, phacoemulsification

Continuous curvilinear capsulorhexis (CCC) is a critical step in phacoemulsification for decreasing the risk of capsule tearing and allowing safe manipulation of the lens.[1,2] In eyes with an advanced (mature or hypermature) cataract, CCC is difficult to perform because of the absence of the red reflex and poor visibility of the anterior capsule.[3,4] Uncertain continuity of the capsulorhexis margin, together with emulsification of a hard nucleus, may lead to various intraoperative complications such as radial tear, zonular dehiscence, posterior capsule rupture, vitreous loss, nucleus drop, and intraocular lens (IOL) displacement. When surgery for advanced cataracts is additionally complicated by the presence of anterior segment abnormalities (such as corneal opacity caused by macular

[1]Department of Ophthalmology and [2]Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

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***Correspondence to:** Dr Sung-Huei Tseng, Department of Ophthalmology, College of Medicine, National Cheng Kung University, 138 Sheng-Li Road, Tainan, Taiwan.
E-mail: shtseng1@gmail.com

Table 1. Characteristics of patients with advanced cataract with (group 1) or without (group 2) pre-existing anterior segment abnormalities*

Patient characteristic	Group 1	Group 2	*p*
Eye (patients)	17 (15)	18 (17)	
Age (yr)	60.0 ± 13.6 (21–73)	69.4 ± 9.6 (50–84)	0.02
Gender (male:female)	8:9	5:13	0.31
Follow-up (mo)	10.4 ± 13.0 (0.4–42.5)	5.0 ± 7.4 (0.1–30.3)	0.13

**Data presented as mean ± standard deviation (range) or n.*

cornea, advanced pterygium, band keratopathy, or previous corneal grafting; small pupils caused by inadequate mydriasis, pupil synechia, or pupil occlusion; or glaucoma), capsulorhexis and the rest of the phacoemulsification procedure will be even more difficult and carry a higher risk of complications.

A number of studies have shown that staining of the anterior capsule with dye, such as indocyanine green (ICG) or trypan blue (TB), helps to visualize the capsular margin during capsulorhexis of a mature/hypermature cataract.[5–20] We are unsure if a dye-enhanced technique would also be helpful during phacoemulsification of advanced cataracts complicated by various anterior segment abnormalities. Therefore, we investigated the rate of intraoperative and postoperative complications and effects on visual acuity of ICG-assisted phacoemulsification in eyes with advanced cataracts, with or without anterior segment abnormalities.

Methods

Patients

The patients were 35 individuals without congenital abnormalities of the eye or adnexa, active uveitis, or retinal or choroidal detachment detected by B-scan ultrasonography, who consecutively underwent phacoemulsification of complicated or simple advanced cataracts performed by the same experienced surgeon (S.H.T.) at National Cheng Kung University in Taiwan between September 2001 and August 2004. Informed consent was obtained from all patients.

Advanced (mature/hypermature) cataract was defined as total lens opacity and lack of a red reflex during capsulorhexis. Complicated or simple cataract was defined as the presence or absence, respectively, of a condition in the anterior segment that could complicate phacoemulsification. Before capsulorhexis, ICG was used to stain the anterior capsule in all patients.

Preoperatively, patients were divided into two groups (Table 1) based on the presence of a complicating condition in the anterior segment. Group 1 consisted of 15 patients (17 eyes) with advanced (mature or hypermature) cataract and at least one of the following conditions: corneal opacity (causes included macular cornea, advanced pterygium, band keratopathy, and previous corneal grafting), small pupil (causes included inadequate mydriasis, pupil synechia, and pupil occlusion), and various types of glaucoma. Group 2 consisted of 17 patients (18 eyes) with an advanced cataract without any significant anterior segment abnormality (Table 2).

Preoperative evaluation

Evaluations performed preoperatively included measurement of best-corrected visual acuity, keratometry, tonometry, axial length, slit-lamp examination to evaluate the severity of the cataract, and B-scan ultrasonography to rule out posterior segment pathology in the eyes with opaque medium that hindered fundoscopic examination.

Dye preparation[5–9]

Immediately before use, 25 mg ICG (Daiichi Pharmaceutical, Tokyo, Japan) was dissolved in 0.5 mL aqueous solvent (provided with the ICG

Table 2. Preoperative ocular manifestations in 17 eyes of group 1 and 18 eyes of group 2*

Ocular manifestation	Group 1†	Group 2
Hypermature white cataract	10 (58.8)	18 (100.0)
Corneal opacity		
Macular cornea	4 (23.5)	0 (0)
Small pterygium	0 (0)	3 (16.7)
Advanced pterygium	2 (11.8)	0 (0)
Band keratopathy	2 (11.8)	0 (0)
Corneal graft	1 (5.9)	0 (0)
Small pupil		
Inadequate mydriasis	3 (17.6)	0 (0)
Pupil synechiae	1 (5.9)	0 (0)
Pupil occlusion	1 (5.9)	0 (0)
Glaucoma		
Phacomorphic glaucoma	2 (11.8)	0 (0)
Phacolytic glaucoma/uveitis	2 (11.8)	0 (0)
Steroid glaucoma	2 (11.8)	0 (0)
Neovascular glaucoma	1 (5.9)	0 (0)
Primary open-angle glaucoma previously undergone trabeculectomy	1 (5.9)	0 (0)

Data presented as n (%); †five patients in group 1 had a combination of corneal opacity, small pupil, and glaucoma.

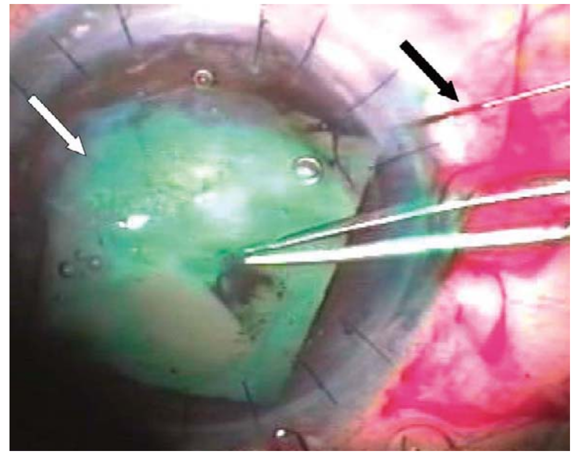

Figure 1. Intraoperative appearance of a complicated advanced cataract after synechiolysis and enlargement of the constricted pupil with iris hooks (black arrow), followed by staining with 0.5% indocyanine green (ICG) to distinguish the anterior capsule (stained light green by ICG) from the underlying white cortex. The scar (white arrow) and constricted pupil were due to previous corneal grafting.

compound). The solution was then mixed with 4.5 mL balanced salt solution (BSS plus®; Alcon, Fort Worth, TX, USA). The final solution contained 0.5% ICG and had an osmolarity of ~270 mOsm/kg.

Surgical technique

Anesthesia was achieved by retrobulbar ganglion block or combined topical/intracameral anesthesia, depending on the patient's ability to fixate on the light of the operating microscope. Mydriasis was achieved by instillation of three successive drops, 5 minutes apart, of Mydrin®-P (0.5% tropicamide and 0.5% phenylephrine hydrochloride; Santen Pharmaceutical Co., Ltd., Osaka, Japan). In eyes with inadequate mydriasis (posterior synechiae, seclusio or occlusio pupillae), a pupil size adequate for the procedure was achieved by synechiolysis and/or placement of an iris retractor (Grieshaber, Switzerland).

A clear corneal incision was made and the aqueous humor was replaced by air. A small amount of the ophthalmic surgical device, Viscoat® (4% sodium chondroitin sulfate/3% sodium hyaluronate; Alcon, Belgium), was injected close to the corneal wound to prevent leakage of air. With a 26-gauge flat cannula, 0.1 mL 0.5% ICG was instilled onto the anterior capsule. The air in the anterior chamber allowed the formation of a "dye lake" over the anterior capsule, bordered by the pupillary margin; it also prevented dilution of the dye by the aqueous humor, so that the lowest effective concentration of ICG was achieved, as described previously.[21,22]

After the dye had been in contact with the capsule for approximately 30 seconds, Viscoat® was injected into the anterior chamber to replace the air. During capsulorhexis, good contrast was seen between the greenish-stained anterior capsule rim and the unstained underlying whitish cortex, even in patients with abnormalities in the anterior segment (Figure 1). The rest of the surgical procedure, including phacoemulsification, irrigation and aspiration of cortex, and IOL implantation, proceeded routinely. Any intraoperative findings or complications were recorded.

Postoperative follow-up

Patients were examined on postoperative days 1 and 3 and at 1 week, 1 month and 3 months after surgery. At each follow-up visit, a complete ophthalmic examination was performed, including measurement of visual acuity, refraction, tonometry, slit-lamp examination, and fundus examination.

Statistical analysis

Data were analyzed using SAS version 9 (SAS Institute Inc., Cary, NC, USA) for statistically significant differences between groups 1 and 2 using Student's t test and Fisher's exact test with the level of significance set at $p < 0.05$.

Results

Table 3 summarizes the anesthetic method used and the adjunctive surgical procedures performed for each patient group. Phacolytic uveitis and absolute glaucoma were diagnosed in one eye in group 1, and thus no IOL was implanted in this eye. The other 34 eyes (16 in group 1, 18 in group 2) underwent routine phacoemulsification and insertion of a foldable IOL using an injector. A noticeable difference between the two groups was that 30% of eyes in group 1 required additional papillary dilatation by iris hooks because of inadequate mydriasis, or synechia or occlusion of the pupil.

The intraoperative and postoperative complications are shown in Table 4. The only significant difference between the two groups was the occurrence of radial tears during the capsulorhexis procedure in four eyes in group 1 ($p < 0.05$). It is noteworthy that radial tears mainly occurred when the lens was tumescent. In these cases, immediately after the first small flap-tear of the anterior capsule had been created with a 25-gauge cystotome needle (Visitec®; BD Ophthalmic Systems, Waltham, MA, USA), a gush of milky cortex rushed out of the opening, followed by the spontaneous occurrence of two radial tears that extended from the center to the lens periphery within a few seconds, because of high intralenticular pressure (Figure 2A). We injected a large bolus of Viscoat® adjacent to the tears to prevent further extension, and then used Vannas scissors to make cuts in the anterior capsule at the peripheral end of each tear to complete capsulorhexis, which resulted in a circular flap with two radial relaxing incisions (Figure 2B). In these four eyes, phacoemulsification and irrigation and aspiration of the cortex were performed with exceptional caution, to avoid extension of the radial tears. In three of these eyes, an IOL was implanted without incident in the ciliary sulcus, with the axis of haptics at 90 degrees to the radial tears; no IOL was placed in the final eye, which was the one

Table 3. Anesthetic and adjunct surgical procedures for phacoemulsification of advanced cataract in 17 eyes with anterior segment abnormalities (group 1) and 18 eyes without (group 2)*

Procedure	Group 1	Group 2	p
Anesthesia (RBGB:T+IC)	7:10	7:11	1.00
Iris hooks to extend the pupil	5 (29.4)	0 (0)	0.02
Bare sclera	2 (11.8)	2 (11.1)	1.00
Calcium plaque removal	1 (5.9)	0 (0)	0.49

Data presented as n or n (%). RBGB = retrobulbar ganglion block; T+IC = combined topical and intracameral anesthesia.

Table 4. Intraoperative and postoperative complications of phacoemulsification of advanced cataracts in 17 eyes with anterior segment abnormalities (group 1) and 18 eyes without (group 2)*

Complication	Group 1	Group 2	p
Intraoperative			
Radial tear	4 (23.5)	0 (0)	0.046
Posterior capsule rupture	0 (0)	0 (0)	–
Vitreous loss	0 (0)	0 (0)	–
IOL displacement	0 (0)	0 (0)	–
Postoperative			
Corneal edema			
Transient	0 (0)	2 (11.2)	0.49
Persistent	1 (5.9)†	0 (0)	0.49
Vitreous prolapse into the anterior chamber and IOL decentration	0 (0)	1 (5.6)	1.00
Posterior capsule opacity	2 (11.8)‡	1 (5.6)‡	0.60
Persistently elevated IOP	2 (11.8)	0 (0)	0.23

**Data presented as n (%); †one patient in group 1 with previous corneal grafting and band keratopathy developed persistent corneal edema and graft failure 2 years later and received another corneal transplant; ‡two patients in group 1 and one patient in group 2 developed posterior capsule opacity within 3 months, for which Nd:YAG capsulotomy was performed. IOL = intraocular lens; IOP = intraocular pressure.*

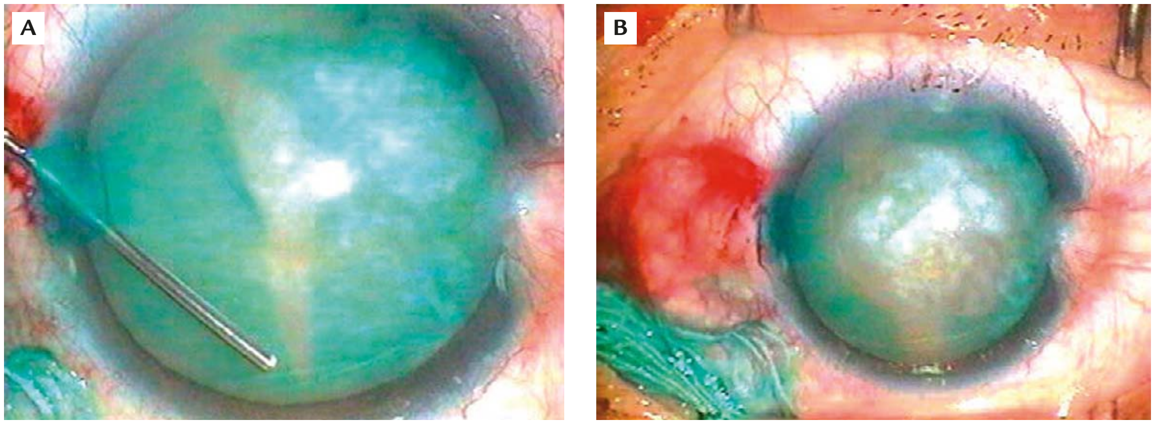

Figure 2. Intraoperative appearance of a complicated advanced cataract after instillation of 0.5% indocyanine green to distinguish the anterior capsule from the underlying white cortex. (A) Immediately after a cystotome had been used to create a small flap-tear of the anterior capsule at the start of capsulorhexis, two radial tears developed spontaneously, from the flap to the periphery, because of high intralenticular pressure. (B) A semicircular capsulorhexis incision was made starting at the peripheral end of each tear, resulting in two semicircular capsulorhexis flaps separated by two radial relaxing incisions.

with absolute glaucoma. There were no other intraoperative complications in either of the groups, specifically no zonular rupture, posterior capsule rupture, vitreous loss, or IOL displacement.

Postoperatively, persistent corneal edema was only seen in one eye. This patient in group 1 previously had corneal grafting, and underwent corneal regrafting 2 years later. On the other hand, mild and transient corneal edema was observed in two eyes in group 2 at 1 week postoperatively, but this resolved completely within 1 month after phacoemulsification. One eye in group 2 had a small amount of vitreous prolapse into the anterior chamber and mild IOL decentration postoperatively but vision was not impaired. Posterior capsule opacity was noted in two eyes in group 1 and one eye in group 2 during the 3-month follow-up period, but Nd:YAG capsulotomy led to improvement in visual acuity in all three of these eyes. Persistently elevated intraocular pressure (IOP) was noted in two eyes in group 1. Preoperatively, one of these eyes had phacolytic uveitis with absolute glaucoma and the other had neovascular glaucoma caused by central retinal vein occlusion.

Figure 3 shows the final visual acuity of patients in groups 1 and 2 as a function of their initial visual acuity. Final visual acuity was improved (at least two lines) in 11 (64.7%) of 17 eyes in group 1 and was unchanged in the other six eyes (35.3%). The six eyes that had no improvement in visual acuity postoperatively had advanced pterygium (one eye), band keratopathy (one eye), absolute glaucoma (one eye), central retinal vein occlusion (one eye), or myopic maculopathy (two eyes). On the other hand, all eyes in group 2 had improved visual acuity (at least two lines) after the operation ($p < 0.01$).

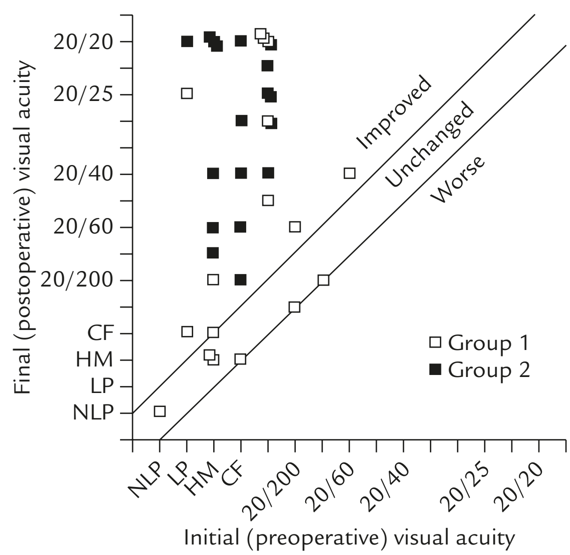

Figure 3. Visual acuity improvement (postoperative as a function of preoperative) after phacoemulsification of advanced cataract in 17 eyes with anterior segment abnormalities (group 1) and 18 eyes without (group 2).

Table 5 shows the distribution of final visual acuity in the two groups of patients. Phacoemulsification of complicated advanced cataract resulted in significantly less favorable outcome with regards to visual acuity than that of simple advanced cataract ($p < 0.01$).

Table 5. Final visual acuity after phacoemulsification of advanced cataract in 17 eyes with anterior segment abnormalities (group 1) and 18 eyes without (group 2)*

Final visual acuity	Group 1	Group 2	*p*
Good (20/40–20/20)	6 (35.3)	14 (77.8)	0.006
Moderate (20/100–20/50)	2 (11.8)	3 (16.7)	
Poor (20/200 or less)	9 (52.9)	1 (5.6)	

*Data presented as n (%).

Discussion

Since the introduction of dye-enhanced capsulorhexis several years ago, CCC in eyes with advanced cataracts is no longer an insurmountable challenge for surgeons.[5–20] Furthermore, in cases of complicated or simple advanced cataracts, instilling ICG to enhance visualization of the capsule margin is safe and effective.

Effectiveness and complications of dye-assisted phacoemulsification in simple advanced cataracts

Two characteristics of advanced cataracts pose challenges for phacoemulsification: the lack of a red reflex to identify the capsule margin during CCC and emulsification of a hard nucleus. A variety of techniques to better visualize the capsular margin have been reported, including dimming the room lights,[23] increasing optical magnification of the operating microscope,[23] side illumination with an endoilluminator,[24] injection of an air bubble into the anterior chamber,[25] two-step CCC,[3,4,26] using a high-frequency diathermy probe and high-density viscoelastic agent,[27] creating a reverse triangular capsulotomy,[28] and aspiration of the cortical material in liquefied cataract,[4] hemocoloration of the capsule with autologous blood,[8,29] and dye-enhanced techniques, including subcapsular or intracameral injection of fluorescein sodium (FS), ICG, TB or gentian violet (GV).[5–20] The most successful of these methods is the dye-enhanced method, and results of studies using these methods are summarized in Table 6.

With the two-step CCC method, the rate of success was 72–95%, and in the study with the higher success rate, the rate of intraoperative complications was 25% (residual cortical debris) to 60% (raised intracapsular pressure), and rates of postoperative complications were 5–20% (Table 6).[3] Reported success rates in studies of dye-enhanced CCC are 94–100% for ICG, 96–100% for TB, 80–100% for FS (only two of five studies reported the CCC success rate), and 100% for two studies of GV (Table 6). The greatest experience with dye-enhanced CCC has been reported for TB (a total of 182 eyes) and ICG (a total of 143 eyes, including the 18 eyes in the present study) (Table 6). In addition to its clinical safety, TB has been shown to be safe and effective for enhancement of visualization of CCC in a rabbit model.[21,22] Furthermore, in our clinical experience (unpublished data), TB works as well as ICG for CCC during phacoemulsification of simple advanced cataracts. In our patients with simple advanced cataracts (group 2), ICG-assisted phacoemulsification was as successful and safe as dye-assisted phacoemulsification reported by others (Table 6).[5,7–11,13–15,19,20]

Effectiveness and complications of dye-assisted phacoemulsification in complicated advanced cataracts

To date, only a limited number of reports have been published regarding the use of dye to assist in CCC for phacoemulsification of complicated advanced cataracts. Bhartiya et al[30] have used TB 0.1% to assist in phacoemulsification of cataracts in 11 eyes with nebulomacular corneal opacities. Use of TB facilitated completion of CCC in all cases, although in one case, phacoemulsification had to be converted to extracapsular cataract extraction because of intraoperative haze. In another series of patients, Baykara et al found that using

Table 6. Summary of studies of phacoemulsification for advanced (mature/hypermature) cataracts with or without assistance of dye

Study (year)	Dye	Technique	Eyes (n)	Successful CCC (%)	Major complications Intraoperative (I)/Postoperative (P)
Vasavada et al. (1998)[3]	None	2-step CCC	60	95	I: raised intracapsular pressure (60%), PCO (33%), residual cortical debris (25%). P: IOP > 26 mmHg (5%), capsular bag contraction (12%), IOL decentration (20%), PCO (5%).
Chakrabarti et al. (2000)[4]	None	2-step CCC	212	72	I: posterior capsule tear (2%), conversion to manual extraction (2%), intraoperative miosis (3%), iris chafing (1%). P: corneal edema (6%), iritis (1%).
Horiguchi et al. (1998)[5]	ICG 0.5%, 1–2 drops	Air bubble	10	100	I/P: none.
Sharma et al. (2001)[6]	ICG 0.5%	Air bubble	25	NR	NR
Yi and Sullivan (2002)[7]	ICG 0.5%, 2–3 drops	Air bubble	33	94	I: posterior capsule rupture with vitreous loss (7%), conversion to ECCE (3%). P: corneal decompensation requiring grafting (3%), cystoid macular edema (3%), choroidal effusion (3%).
Dada et al. (2004)[8]	ICG 0.5%, 0.1 mL	Air bubble	10	100	I/P: none.
Xiao et al. (2004)[9]	ICG 0.5%	Air bubble	30	97	I: ICG staining in anterior vitreous (3%). P: corneal edema on day 1 (37%).
Chung et al. (2005)[10]	ICG 0.5%, 0.5 mL	Air bubble	17	NR	I: none. P: mild corneal haziness at 1 month (12%).
Current study (2008)	ICG 0.5%, 0.1 mL	Air bubble	18	100	I: none. P: mild corneal edema at 1 week postoperatively (11%), vitreous prolapse and mild IOL decentration (6%), PCO (6%).
Melles et al. (1999)[11]	TB 0.1%, 0.1 mL	Air bubble	30	100	I/P: none.
Yetik et al. (2002)[12]	TB 0.00625–0.1%, 0.1 mL	Air bubble/ under Viscoat	35	NR	NR
Jacob et al. (2002)[13]	TB 0.06%	Air bubble	52	96	I: conversion to ECCE (4%), intraoperative miosis (4%). P: corneal edema (6%), anterior chamber inflammation (12%), IOP > 24 mmHg (8%).
Toprak et al. (2003)[14]	TB 0.1%	Air bubble with a modified cannula	6	100	I: zonular dialysis (17%).
Singh et al. (2003)[15]	TB 0.06%, < 0.5 mL	Air bubble	10	100	I: none.
Dada et al. (2004)[8]	TB 0.1%, 0.1 mL	Air bubble	10	100	I/P: none.
Xiao et al. (2004)[9]	TB 0.1%	Air bubble	25	100	I: none. P: corneal edema on day 1 (32%).
Chung et al. (2005)[10]	TB 0.1%, 0.5 mL	Air bubble	14	NR	I/P: none.
Hoffer & McFarland (1993)[16]	FS	Subcapsular injection	NR	NR	NR
Gotzaridis & Ayliffe (1995)[17]	FS 2%, 1 drop	Under Ocucoat	12	NR	NR
Nahra & Castilla (1998)[18]	FS 1%, 0.1 mL	Air bubble	NR	NR	NR
Fritz (1998)[19]	FS, 0.05–0.1 mL	Subcapsular injection with blue filter	7	100	I: posterior capsule rupture (29%).
Dada et al. (2004)[8]	FS 2%, 0.01 mL	Subcapsular injection	10	80	I/P: none.
Ünlű et al. (2000)[20]	GV 0.001%/0.01%, 0.05 mL	Air bubble	18	100	I/P: none.
Dada et al. (2004)[8]	GV 0.001%, 0.1 mL	Air bubble	10	100	I/P: none.

PCO = posterior capsular opacity; IOP = intraocular pressure; IOL = intraocular lens; NR = not reported; ECCE = extracapsular cataract extraction; ICG = indocyanine green; Viscoat = 4% sodium chondroitin sulfate/3% sodium hyaluronate; Ocucoat = methylcellulose.

0.1% TB to stain the anterior capsule facilitated successful capsulorhexis in 10 patients with traumatic swollen lens due to perforating eye injuries.[31] Kobayashi et al have used 0.5% ICG successfully in four cases undergoing a triple procedure; the dye was applied to the anterior capsule after trephination and facilitated successful CCC in all four cases.[32]

In the present study of ICG-assisted phacoemulsification in 17 patients with advanced cataracts, complicated by a variety of anterior segment abnormalities, ICG was as safe and effective for CCC as in previous studies of TB or ICG used for complicated advanced cataracts.[30–32] In our experience, use of dye is almost required to achieve a perfect CCC and uneventful phacoemulsification of advanced cataracts in eyes with anterior segment abnormalities such as corneal opacity, small pupil, or glaucoma.

Comparison of dye-assisted phacoemulsification for complicated versus simple advanced cataracts

With regard to ethics and the difficulty of performing phacoemulsification in eyes with advanced cataracts complicated by anterior segment abnormalities, we chose to compare the use of dye in patients with simple versus complicated advanced cataracts, rather than comparing use or no use of dye in patients with complicated advanced cataracts. Although our results showed that applying ICG dye to the anterior capsule was safe in all cases of advanced cataract and very helpful in CCC for phacoemulsification of advanced cataracts in eyes with co-existing anterior segment abnormalities, great caution should be exercised during all stages of surgery in these latter cases.

Except for the presence of anterior segment abnormality, the only significant difference preoperatively between group 1 and group 2 patients in this study was age (Table 1). This difference is explained by the fact that simple advanced cataracts are more frequently seen in older patients, whereas complicated advanced cataracts may occur in patients of any age who have an underlying ocular or systemic disease. The age difference between the two groups may have resulted in a bias toward being over-conservative for the main outcomes, such as intraoperative/postoperative complications and final visual acuity.

One significant difference between groups 1 and 2 in our study was that an iris hook was needed to extend the pupil in five (29.4%) eyes with complicated advanced cataract, but not in any of the eyes with simple advanced cataract. However, the proportion of eyes in each group that required a bare sclera technique or removal of calcium plaque was similar (Table 3).

As shown in Table 4, groups 1 and 2 also differed in the rate of radial tear, which occurred in four (23.5%) eyes in group 1 versus none in group 2. Radial tear was most often caused by the lens being swollen and was not related to the use of dye. To decrease the risk of radial tear, Gimbel advocated a two-stage CCC or aspiration of the milky cortex before CCC.[26] If only one radial tear occurs, capsulorhexis can be continued after making a snip cut to create a new flap. Similarly, if a large horizontal tear occurs and extends to the periphery on both sides, two semicircular CCCs can be created, as shown in Figure 2. However, phacoemulsification must be performed with extreme caution to prevent extension of the tear to the posterior capsule, and the IOL should be placed in the sulcus with the haptics oriented at 90 degrees to the radial tear, especially when complicated by posterior capsular rupture.

With regard to postoperative complications, groups 1 and 2 did not differ significantly (Table 4), and none of the complications was related to the use of ICG. Transient corneal edema occurred in two eyes in group 2 after phacoemulsification of simple advanced cataract. The edema in these cases might have been caused by high phaco power, prolonged time to complete phacoemulsification, and/or extended manipulation of the hard lens. Except for persistent corneal edema (delayed corneal decompensation) that occurred in an eye with previous corneal graft, our series showed that ICG did not induce significant corneal endothelial injury, macular edema, or other retinal injuries. Postoperative vitreous prolapse and IOL decentration that occurred in one eye in group 2 might have been caused by subclinical or iatrogenic zonular dehiscence. Early development of posterior capsule opacity (two eyes in group 1 and one in group 2) might have resulted from hidden residual lens fibers. The persistent elevation of IOP in two eyes in group 1 was related to pre-existing glaucoma.

The differences between groups 1 and 2 in improvement in postoperative visual acuity were related to limitations in improvement in group 1 caused by the nature of pre-existing ocular conditions. In addition, age difference between groups may have influenced our results. If older age was related to a worse surgical condition or prognosis, the outcome in the simple advanced cataract group would have been intrinsically worse than that in the complicated advanced cataract group. This might reduce the significant level we can observe for our main outcomes, including intraoperative or postoperative complications, and final visual acuity. Our results showed a statistical significance in the rate of intraoperative radial tear and in the final visual acuity but no difference in the rate of postoperative complications. If patient age in the two groups was matched, the rate of postoperative complications might become more statistically different. A future study with matched demographic features will be able to eliminate such a confounding factor and bias in the results.

Choice of dye for dye-assisted phacoemulsification

As shown in Table 6, clinical studies have been conducted on four dyes (ICG, TB, FS, GV) to assist with phacoemulsification. Our previous study has investigated various concentrations of these dyes and methylene blue (MB) in a rabbit model[21] and no cytotoxic effects were observed after 1 minute exposure to 0.25% ICG, 0.20% MB, 0.01% GV, 0.40% TB, or 10% FS, whereas cytotoxicity was observed after 1 minute of exposure to 0.50% ICG, 0.50% MB, or 0.10% GV. Furthermore, the lowest effective concentration for anterior capsule staining was 0.25% ICG, 0.10% MB, 0.01% GV, 0.10% TB and 1.25% FS.[22] Pandey et al reported that, in postmortem eyes, the staining quality provided by 0.5% ICG was slightly superior to that provided by 0.1% TB or 2% FS.[23] In a recent clinical study that compared different dyes for phacoemulsification of white cataracts,[8] 0.1% TB, 0.5% ICG and 0.001% GV were more effective in staining the anterior capsule than 2% FS or autologous blood. In another comparative study,[9] the staining provided by 0.1% TB was reported to be slightly superior to that provided by 0.5% ICG.

The concentration of ICG generally used for cataract surgery is 0.5%,[5–10] which raises a clinical concern of corneal endothelial toxicity. In the limited number of relevant studies to date, Horiguchi et al[5] and Chung et al[10] reported no significant difference in corneal endothelial cell counts between patients with or without use of ICG in capsulorhexis. Although we found that 0.5% ICG damaged rabbit cultured corneal endothelial cells within 1 minute of exposure,[21] this result can not be directly extrapolated to clinical practice. Theoretically, corneal endothelial cells *in vivo* should be more resistant than cultured cells for four reasons. First, the amount of ICG used is limited. Second, the duration of exposure clinically is generally less than 1 minute. Third, direct contact of ICG with the corneal endothelium is prevented by an air bubble. Fourth, the proteins and buffered ions in the aqueous humor offer some protection against the toxic effects of ICG.

The case numbers in our study were limited; therefore, we recommend larger-scale clinical trials and quantitative measurement of corneal endothelial counts by specular microscopy to compare the efficacy and safety of various dyes for phacoemulsification of advanced cataracts.

The present study, believed to be the first to investigate the feasibility of ICG-assisted phacoemulsification in eyes with complicated or simple advanced cataracts, showed that staining the anterior capsule with 0.5% ICG facilitates visualization of the capsule during phacoemulsification, particularly when there is an anterior segment abnormality such as corneal opacity, small pupil, or glaucoma, and is not associated with any adverse effects. Although patients with complicated advanced cataracts had a higher incidence of radial tear of the anterior capsule and less improvement of final visual acuity, these differences resulted from underlying causes of complicated advanced cataracts, and were not related to ICG use.

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